RECOVERY OF NORMAL AND ECZEMATOUS SKIN FROM ALKALI

Control of Surface pH by Exchange Resins*

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Exposure of the skin to alkalis, such as soap solutions, cement or plaster, results in large displacements of skin pH, and this often gives rise to a dermatitis or continues or aggravates an existing one. Dermatologists know from clinical experience and the laboratory shows resistance to alkali varies within wide limits among patients with cutaneous irritations as well as with those with apparently normal skin. Burckhardt (1) showed persons with alkali dermatitis have less ability to combat alkali in that it takes them longer to regain the normal skin acidity after exposure to basic materials. It would seem desirable to extend our fundamental knowledge on the behavior of the normal and pathological skin toward alkali, to differentiate normal from the apparently normal skin in their potential alkali capacities and find means to improve the performance of all skin exposed to this common hazard.

The history of dermatologic therapy is a record of means to protect the skin from noxious agents and of course to heal it after injury. Mostly we find attempts to build barriers to keep out invaders. One of the best known is Lassar's paste designed to ward off outside irritants as well as to interfere little with the cutaneous activities, such as disposing of secretions, exudates and discharges. Latterly many pharmaceutists hailed the virtues of a new group of chemicals, the silicones, for their capacities to fulfill just this role. These silicone derivatives are profoundly inert and would seem to be ideal for defending the skin against alkali and irritants. They make up into pleasing preparations, easy to use, with surprisingly long lasting presence after application, and little or no untoward effects. Opinion about their effectiveness still remains uncrystallized, but some dermatologists of experience find these new agents fall short of promises and expectations. We must not relax our efforts to seek other measures than these defensive ones. Perhaps we may find more aggressive ones to neutralize and destroy the sting of irritants such as alkali.

Recent therapeutic development provided us with new kinds of inert agents with the power to take or give up ions unwanted or needed whichever the case demands. They themselves, as in the case of catalysts, remain intact. Thus far they are used medicinally only in internal medicine, such as for taking up sodium in dropsical states. They are now widely used in industry and sanitation, as for water purifications. These newer agents are the ion-exchange resins. They may be designed to accomplish various purposes depending upon what the situation needs. We thought one that could furnish hydrogen or take up hydroxyl ions

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might be useful and of value in combatting the ill effects of exposure of the skin to alkali. We found several for trial and in this communication record our experimental experiences with them.

METHOD

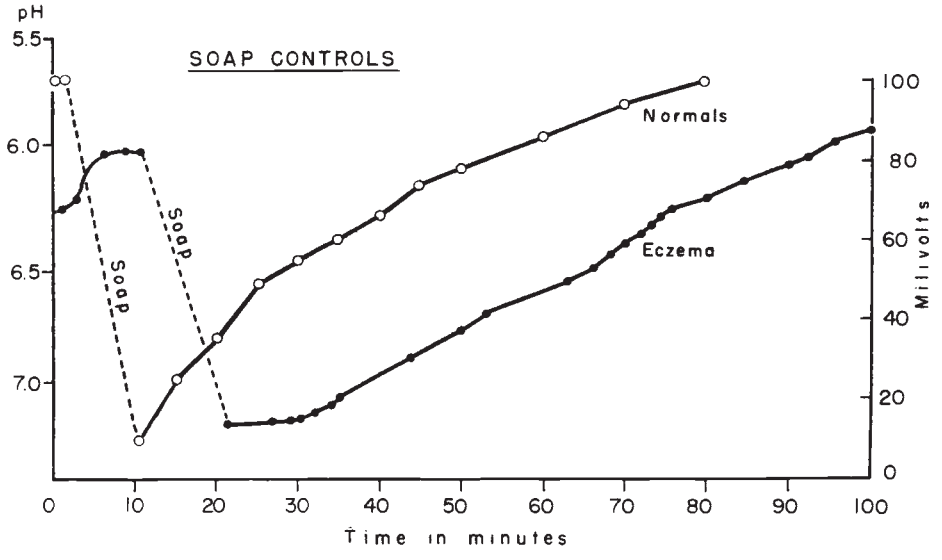
Both normal persons and those with atopic eczema were used to determine the initial pH of the skin of the dorsal surface of the hand potentiometrically with the quinhydrone electrode. The hand was then immersed and moved actively in a saturated solution of Penick's white, powdered castile soap, U.S.P., for 10 minutes. The pH of the soap solution was 9.0. The excess soap on the hand was wiped off with a towel. About 1 cc. of saturated quinhydrone in isotonic NaCl solution was put into a glass cylinder with one end resting on the skin. Determinations were made every minute and a curve of recovery was determined. Similar recovery curves were determined following application of very dilute NaOH solutions. Normal persons and patients with atopic eczema were compared using various concentrations of solution. Following recovery of the initial pH, cation exchange resin was applied to the area of the hand under test. A thin film was used and any excess wiped away. The procedure for pH recovery was repeated. Certain variations in the procedure were also studied. For example, resin was applied before and after soap immersion. In some experiments resin was applied only before, in others only afterwards and in still others both before and afterwards. The effects of multiple applications of resin were observed. In all sets of experiments behavior of patients with atopic eczema was compared with that of normal subjects.

RESULTS

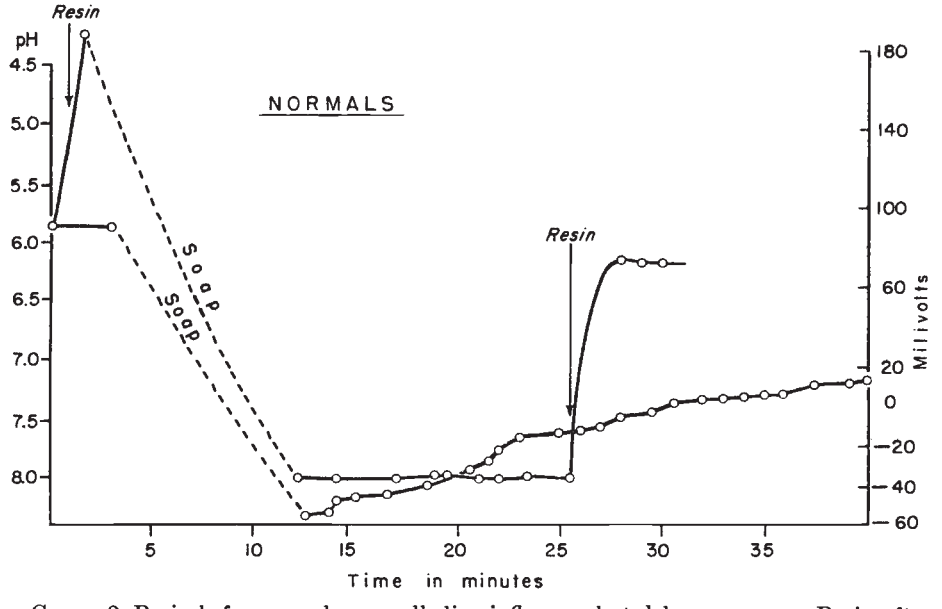
All measuring equilibria take longer to reach on skin of atopic eczema. It took 11 minutes to obtain the control pH value before soaping (Graph 1). The pH of the normal skin is more acid than that of eczematics. Immersion in the same soap solution brought both sets of subjects to about the same pH, but depressed the normals a greater distance from their starting point. Recovery of normals is more rapid after soaping. After 20 minutes they are almost half way to full recovery, whereas the eczema group has made little. Thus, skin of atopic eczema remains relatively alkaline for a longer time than normal skin and whatever harmful influences deprivation of an acid coating have on skin are there a longer time to exert themselves. Recovery from alkali in normals and those with eczema show rebound—the skin becomes more acid than it was at the start, then finally finds its initial pH. This rebound effect is greater in eczema than with normals.

A hydrogen ion-donating resin* when put on the normal skin makes the surface more acid (Graph 2). If now such resined skin is immersed in soap solution for 10 minutes, it does not become quite as alkaline as skin that had no previous application of resin. Resin applied to skin before soaping retards and even pre-

* Dr. Harvey Blank of The Squibb Institute furnished us with the resin, a 15 per cent cationic exchange resin ointment with a hydrocarbon gel base (4-AAM-1).



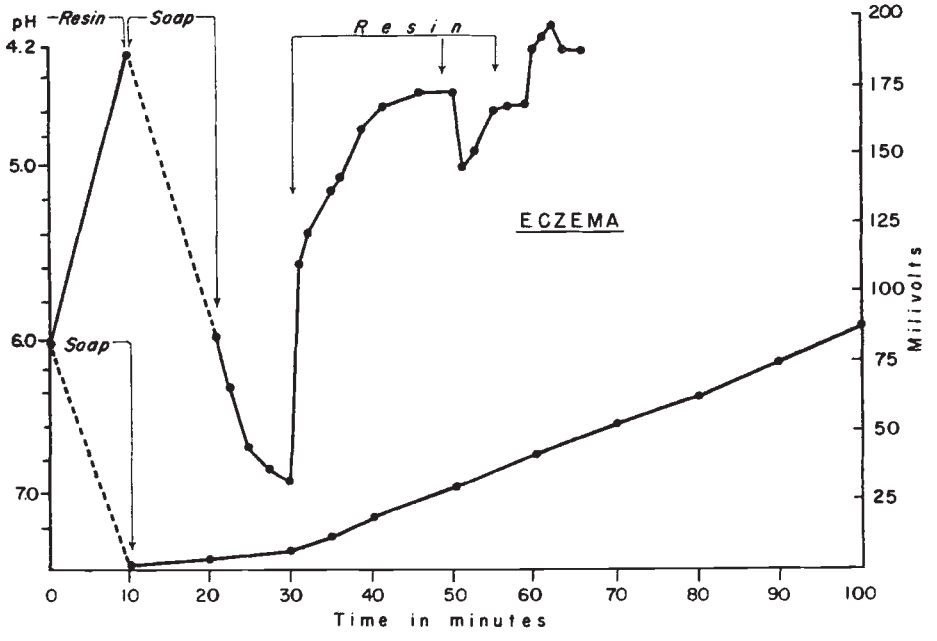
GRAPH 1. Soap controls. With eczema recovery is slower and influence of alkali is more intense and lasts longer.



GRAPH 2. Resin before soap lessens alkaline influence, but delays recovery. Resin after soap hastens recovery.

vents recovery from the alkaline phase. If resin is applied again to the skin at this point immediate recovery to the acid state occurs.

In atopic eczema the use of resin makes the skin markedly acid (Graph 3). Immersion in soap then increases its pH, but this alkaline effect of soap is de-



GRAPH 3. Resin before soap moderates alkaline influence, but delays recovery. Resin after soap hastens recovery. Larger amplitudes present in eczema.

creased by the previous use of resin. It takes a prolonged interval before the full alkaline effects are measurable. There is a delay in recovery with the use of resin before soap, but repetition of resin after the soap hastens recovery to the acid state. The fluctuations from the acid to alkaline states and back again induced by soap and resin are greater in ezema than in normals.

DISCUSSION

The efficiency of amberlite in contributing to control of pH depends on its cation exchange properties. Essentially it is one of the two or three cation exchanges systems in dynamic equilibrium, the others are the base-binding colloids of the epidermis and the applied soap solution. Any free base tends to be distributed in an equilibrium involving all the base-binding colloids. The pH of the supernatant liquid in equilibrium with these systems thus depends on the degree of saturation of the various colloids with base. The principles governing this equilibrium may be briefly outlined. Let HR denote the amount of resin available for combination with base B, and let BR denote the basic complex formed.

Then

$$HR + BOH = BR + H_2O.$$

Similiarly, if BS denotes the soap, and BC the base binding groups of the skin, then

$$HS + BOH = BS + H_2O$$

and

$$HC + BOH = BC + H_2O.$$

If the three systems are at equilibrium, and at a common pH, the reaction is determined by the relations

$$\begin{aligned} pH &= pK_1 + \log \frac{BR}{HR} \\ &= pK_2 + \log \frac{BS}{HS} \\ &= pK_3 + \log \frac{BC}{HC}. \end{aligned}$$

The three ratios representing the degrees of saturation of each of the colloids with base depend on the pH and the three constants, pK_1, pK_2, and pK_3.

If for given quantities of S, C, and B, the total amount of resin, R, is varied, the pH depends on the degree of saturation of the resin. As resin is added, base is taken up from both the skin colloids and the soap. Accordingly, the greatest possible decrease occurs when the ratio of BR to HR is small, that is when a large excess of resin is present. Small quantities of resin, on the other hand, while preventing excessive increases of pH, retard the normal rate of fall of pH ensuing on removal of the hand from soap solution. When the resin is saturated with base the pH of the supernatant liquid is high. This does not fall until the excess base is removed from the resin by exchange with the skin colloids, and subsequent transference to deeper structures or to the circulation. Thus the base retained by the resin constitutes an additional quantity which must ultimately be removed by physiological mechanisms. Under these conditions, the resin delays the recovery of normal skin pH, following immersion of the resined hand in soap solution.

The effect is quite different when an excess of pure uncombined resin HR is applied subsequent to rinsing the hand in soap. Under these conditions the ratio of BR to HR is small, and a rapid fall of pH ensues. Optimal results are obtained when resin is applied before immersing the hand in soap, the alkaline resin, BR, is completely removed after removing the hand, and an excess of pure resin is then applied. In this procedure the surface of the hand is protected during immersion from high pH of the soap solution, while removal of the saturated resin BR and application of pure resin HR produces a rapid decrease in the ratio of BR to HR, and a concomitant rapid decrease of pH.

In these processes the properties of the skin colloids are of importance. These colloids consist largely of keratin, of free mucopolysaccharides and glycoproteins. The base binding properties depend on all these moieties. Of these components the mucopolysaccharides, such as hyaluronic acid and chondroitin sulfuric acid are the fractions with the lowest base binding equivalent weights. Therefore, gram for gram, they bind far more base than keratin, which is a colloid with a high equivalent weight. It follows that the mucopolysaccharides contribute a large fraction of the base binding colloids of skin and that there is a

high correlation between the pH of the skin and the base bound to these acidic residues. The mechanical and structural characteristics of the skin probably depend to a large extent on the state of aggregation of the colloids. When this is high, the skin might be expected to be tight and dehydrated, with a high base binding capacity. Under conditions of depolymerization the water content of the skin would be high, the base binding and buffering capacity would be low, and the surface structures soft and flaccid. The mechanical and physicochemical properties of the system are under endocrine control and appear to vary in pathological conditions.

Thus, in a patient with eczema our experimental evidence indicates poor buffering and low base binding capacity of the skin colloids, attributable to the disease process. Normal subjects showed less abrupt changes of pH ensuing upon applications of resin or soap, under the various experimental procedures.

Normally, the physicochemical properties of the skin vary also under conditions of stress such as emotional states or drastic change of the environment. For example, unpublished evidence indicate that seasonal variations occur indicating changes from summer to winter.

SUMMARY

The behavior of normals and persons with atopic eczema to contact with alkali was studied by potentiometric determinations of the reaction of their skin.

Cationic exchange resins were employed to modify the effects of alkali and soap on the skin.

Compared with that of normals it was found atopic skin shows greater fluctuations in the alkali-acid reaction curve. It takes longer for skin of atopic eczema to establish an equilibrium and to recover from alkali, so that such skin remains under the influence of alkali longer. Hydrogen donating resin applied to the skin after contact with alkali and soap promptly acidifies the surface. Resin applied only before use of alkali prevents extensive increase of pH, but may delay recovery to the acid state. Resin before and afterwards both prevents extreme alkalization and hastens recovery. The physicochemical system of colloidal equilibrium as exerted by the mucopolysaccharides of the skin and keratin is briefly discussed.

REFERENCE

1. Burckhardt, W.: New investigations on skin sensitivity to alkalis. Dermatologica, 94: 73, 1947.

DISCUSSION

Dr. Donald M. Pillsbury, *Philadelphia, Pa.:* I really hadn't intended to discuss this paper, but Dr. Cornbleet started off with a couple of premises with which I didn't agree. I am not at all sure that the premise that the aggravation of dermatitis by soap is due to the higher pH, is correct.

Also I don't—while it is in the literature and is generally accepted—agree

that Burckhardt proved beyond any doubt that the dermatitis of his patients were related to failure of the skin to neutralize alkali. Dr. Cornbleet's method was much more precise than the one used by Burckhardt, but the clinical significance of these findings is not clearcut.

I think we should be very careful not to accept the acid mantle theory too readily. It is an attractive theory, and lends itself nicely to advertising copy, but we must remember that the intact stratum corneum is enormously resistant to very wide changes in pH, from minus 2.0 to 12.5 or so, for forty-eight hours or more. The non-intact stratum corneum is reasonably resistant, though not as much so. But we have no real evidence that these moderate variations from pH 4.5 to 7.5 really have any bad effects on either the intact or the non-intact stratum corneum.

Van Scott and Lyon, working in our department, found that the denaturing effect of detergents was not dependent on the pH. Often we have argued that a particular eruption localized in the area because that area had a high pH. We were measuring an end effect in that area, not something necessarily of etiologic significance. It has been argued that certain bacteria or yeast localize in areas with a high pH, and yet we find that some strains of micrococci which are found in enormous numbers on the skin, will not grow *in vitro* at the normal pH levels of the skin surface. I think we therefore must be extremely careful in interpreting these data as to the clinical effects of the ion exchange resins in terms of pH changes.

When these compounds became available they were most interesting theoretically, and a lot of speculation arose in our own minds. But they have not been very helpful clinically, in fact we have been unable to demonstrate any effects not attributable to those of a standard bland drying lotion.

DR. CORNBLEET (in closing): As Dr. Pillsbury knows, I have been one with him to question the all-importance of the acid-mantle theory. We need a good deal more work to be done to settle some of these matters. All that our present work shows is that the skin of eczema subjects, both at involved and uninvolved sites, does not neutralize alkali as rapidly as that of normal individuals, and the former remains under the influence of alkali longer after an exposure and the degree of alkalization is greater. In these senses, people with eczema are less able to defend themselves against the effects of soap. Undoubtedly some subjects can overcome the influence of soap and return to equilibrium approximately as well as normal persons do.